

## MAGNETIC POLYSACCHARIDE NANOSPHERES WITH POTENTIAL FOR BIOMEDICAL APPLICATIONS: PREPARATION VIA A REVERSE MINIEMULSION METHOD

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Magnetic polymeric supports such as micro- and nanospheres have attracted increasing interest in the last few years due to their potential for applications in biology and medicine, such as cell isolation, protein immobilization, targeting drug delivery and clinical diagnosis [1]. For use in biomedical applications, magnetic polymer nanospheres need to fulfill some requirements: biocompatibility, narrow size distribution and high density of reactive surface groups for the coupling of active biomolecules. In addition, nanospheres should have high and uniformly dispersed magnetic content with superparamagnetic behavior. In our previous work [2]  $\kappa$ -carrageenan, a non-toxic sulphated polysaccharide has been successfully employed as a colloidal stabilizer in the in-situ synthesis of superparamagnetic magnetite nanoparticles, preventing their spontaneous agglomeration and conferring biocompatibility to the resulting composite. Moreover, the resulting ferrofluid, that contained magnetite nanoparticles prepared by co-precipitation within the  $\kappa$ -carrageenan under alkaline conditions, could undergo gelation under cooling conditions due to the gelling properties of this biopolymer.

In this work, taking advantage of the ability of the ferrofluid to form gels, composite nanospheres consisting of magnetite nanoparticles embedded in a  $\kappa$ -carrageenan matrix have been prepared for the first time, using reverse miniemulsions. The reverse miniemulsions were obtained by sonication of a quaternary system comprising n-heptane as the organic phase, cetyltrimethylammonium bromide (CTAB) as surfactant and 1-butanol as the co-surfactant. The aqueous phase consisted on the ferrofluid containing the biopolymer and magnetite nanoparticles ( $d \sim 8$ nm). The stability of the miniemulsion was seen to be affected by the fine composition of the aqueous phase, namely by the concentration of alkali-metal cation added for magnetite precipitation.

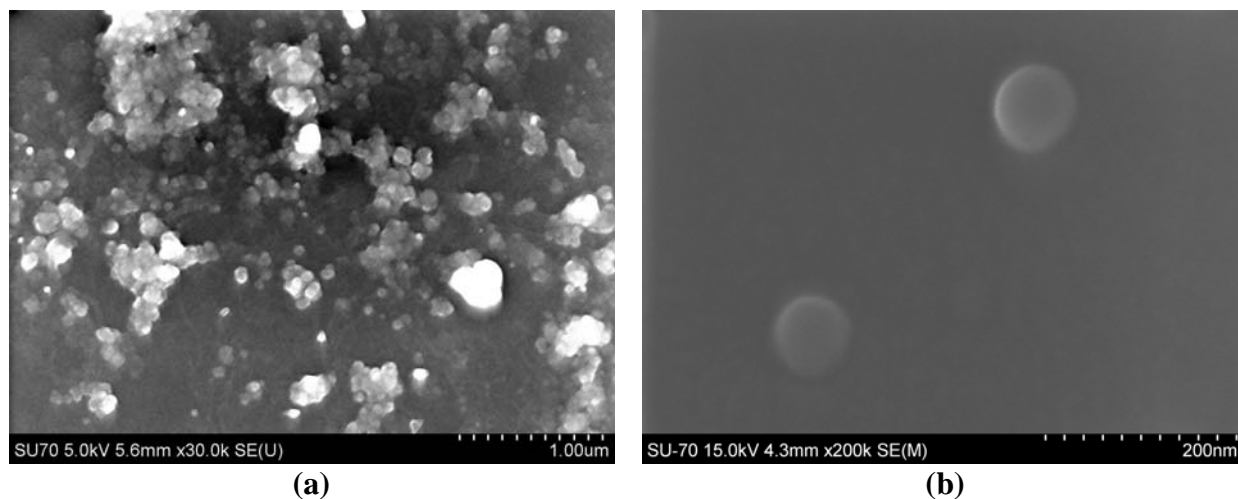
Using the method outlined above, stable miniemulsions containing the magnetic polymeric fluid as aqueous phase were successfully obtained. The spherical morphology of the resulting polymer nanocomposites was confirmed by scanning electron microscopy (SEM), with particles showing an average diameter of 75 nm (Fig.1). DLS measurements have shown larger sizes than SEM probably due to some magnetic interaction of the spheres to form aggregates in solution. The control of the average size of the nanospheres was seen to be possible upon the variation of the concentration of surfactant. Furthermore, magnetic measurements have shown that magnetite nanoparticles are superparamagnetic at ambient temperature (Fig. 2).

The resulting composites are, therefore, of potential interest for several biomedical applications. Since  $\kappa$ -carrageenan forms thermoreversible gels, the controlled release of magnetic particles or loaded drugs can be envisaged by both thermal and magnetic stimuli. In addition, carrageenan can be further functionalized for the conjugation of biomolecules on the surface of the nanospheres, which is the subject of ongoing work.

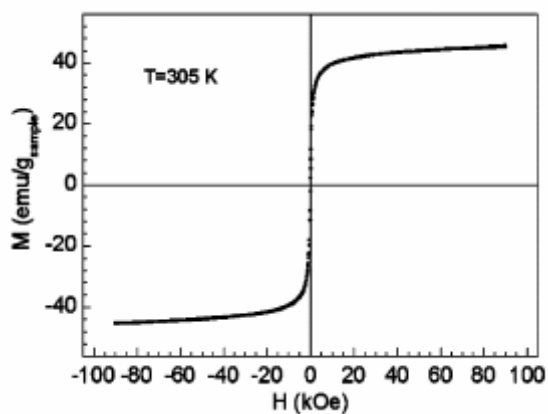
### References:

- [1] U. Hafeli, W. Schutt, J. Teller, M. Zborowski, Scientific and Clinical Applications of Magnetic Carriers, Plenum, New York, 1997.
- [2] A.L.Daniel-da-Silva, T. Trindade, B.J. Goodfellow, B.F.O. Costa, R.N. Correia, A.M. Gil,

**Figures:**



**Figure 1.** SEM images of magnetic nanospheres at different magnification (a) 30,000 $\times$ ; (b) 200,000 $\times$ .



**Figure 2.** Magnetization as function of magnetic field at 305K.